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10/606,618	06/26/2003	Ralph C. Judd	UM/SBC147BUSA	4915

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,618	JUDD ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,30-36,39-42,44-46,50,52 and 55-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,30-36,39-42,44-46,50,52 and 55-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *021408*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 02/14/08 has been entered.

Applicants' Amendments

2) Acknowledgment is made of Applicants' amendments filed 05/01/08 and 02/14/08 in response to the final Office Action mailed 08/14/07.

Status of Claims

3) Claims 43, 51 and 53 have been canceled via the amendment filed 02/14/08.

Claims 25, 32, 34, 42, 44, 50 and 52 have been amended via the amendment filed 02/14/08.

New claim 55 has been added via the amendment filed 02/14/08.

Claims 50 and 55 have been amended via the amendment filed 05/01/08.

New claims 56-58 have been added via the amendment filed 05/01/08.

Claims 25, 30-36, 39-42, 44-46, 50, 52 and 55-58 are pending and are under examination.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' Information Disclosure Statement filed 06/12/07. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

6) The rejection of claims 43 and 51 made in paragraph 38 of the Office Action mailed 12/15/06 and maintained in paragraph 15 of the Office Action mailed 08/14/07 under 35 U.S.C §

first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claims.

7) The rejection of claim 53 made in paragraph 41 of the Office Action mailed 12/15/06 and maintained in paragraph 16 of the Office Action mailed 08/14/07 under 35 U.S.C § 102(b) as being anticipated by Manning *et al.* (*Microb. Pathogenesis*. 25: 11-22, July 1998, already of record) (Manning *et al.*, 1998) in light of Richarme *et al.* (*Ann. Microbiol.* 133A: 199-204, 1982, already of record), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

8) The rejection of claims 30-36, 50 and 52 made in paragraph 41 of the Office Action mailed 12/15/06 and maintained in paragraph 16 of the Office Action mailed 08/14/07 under 35 U.S.C § 102(b) as being anticipated by Manning *et al.* (*Microb. Pathogenesis* 25: 11-22, July 1998, already of record) (Manning *et al.*, 1998) in light of Richarme *et al.* (*Ann. Microbiol.* 133A: 199-204, 1982, already of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

Rejection(s) Maintained

9) The rejection of claims 25, 39-42 and 44-46 made in paragraph 41 of the Office Action mailed 12/15/06 and maintained in paragraph 16 of the Office Action mailed 08/14/07 under 35 U.S.C § 102(b) as being anticipated by Manning *et al.* (*Microb. Pathogenesis*. 25: 11-22, July 1998, already of record) (Manning *et al.*, 1998) in light of Richarme *et al.* (*Ann. Microbiol.* 133A: 199-204, 1982, already of record), is maintained for the reasons set forth therein and herein below.

New claims 55, 56 and 58 are now added to this rejection, because the polypeptide contained in the prior art composition is structurally identical to the instantly recited polypeptide. Because the prior art polypeptide is structurally identical to the instantly recited polypeptide, it is expected to necessarily have the same functional properties of the instantly recited polypeptide, i.e., the ability to induce antibodies in a mammal that bind to the amino acid sequence of SEQ ID NO: 4 that interfere with the ability of *Neisseria* bacteria to adhere to mammalian cells.

New claims 55, 56 and 58 have the effective filing date of the instant application due to the new matter identified below.

Double Patenting Rejection

10) Claims 50, 55, 30 and 31 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1 and 2 of the U.S. patent 6,610,306 (Applicants' IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other because the immunogenic composition of claims 1 and 2 of the U.S. patent 6,610,306 falls within the scope of the instant claims, since the instantly recited polypeptide of SEQ ID NO: 4 is encompassed therein.

Rejection(s) under 35 U.S.C § 112, First Paragraph

11) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

12) Claim 25 and the dependent claims 39-42 and 44-46 are rejected under 35 U.S.C § first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 25, as amended, includes the new limitations: having an amino acid of 95% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4, or having an amino acid sequence which comprises 'an epitope of said SEQ ID NO: 4'. The new limitation 'an epitope of said SEQ ID NO: 4' has no size and/or structure limit, but is required to have diagnostic function, i.e., diagnosis of an unspecified disease or condition. The term 'epitope' encompasses a contiguous epitope and a discontiguous epitope, a linear epitope and a conformational epitope, and a B-cell epitope and a T-cell epitope. Applicants state that lines 25-29 of page 25 of the specification provide support for the limitation of an epitope of the Omp85 sequences. Applicants assert that there is description of an epitope of OMP85, e.g., the exemplary N-terminal sequence used to generate antibodies used, in the examples. Applicants further submit that the specification at page 29, line 16 to page 30, line 5 describes the use of such OMP85 antigenic polypeptides as diagnostic reagents. Applicants also point to page 20, lines 26-29; page 26, line 14 through page 27, line 2; page 35, lines 7-10; page 52,

line 29 through page 53, line 7; and Figure 6 for descriptive support. However, these parts of the specification do not provide support for a generic 'epitope of SEQ ID NO: 4' of any generic contiguous or discontiguous structure and of any limitless size. The epitope described in the paragraph bridging pages 20 and 21 of the instant specification is limited to a fragment of the Omp85 of the instant invention that is about 5 to 8 amino acids in length. The exemplary N-terminal sequence specifically used to generate antibodies in the examples of the instant specification is 178 amino acids in length. Therefore, 'an epitope of said SEQ ID NO: 4' of no particular size, but of generic diagnostic significance is new matter. Furthermore, although claim 25 is drawn to a diagnostic composition comprising a labeled polypeptide as recited, the dependent claim 44-46 require that this labeled diagnostic polypeptide composition 'induce antibodies which recognize a protein in multiple *Neisseria gonorrhoeae* strains (FA19, FA635, FA1090, JS1, MS11 and F62) and *Neisseria meningitdis* strains (HH, MP78, MP3 and MP81)'. This means that the labeled diagnostic polypeptide composition of dependent claims 44-46 is required to be 'immunogenic' as well, being capable of inducing broadly cross-reactive antibodies. Induction of such antibodies requires the *in vivo* administration of the labeled diagnostic polypeptide composition to a human or animal, for which there is no descriptive support in the instant specification. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the new limitation(s), or alternatively remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

13) Claim 55, 56 and the dependent claim 58 are rejected under 35 U.S.C § first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 55 includes the limitations: 'immunogenic composition comprising an isolated polypeptide ……. said polypeptide comprising an epitope of at least 8 consecutive amino acids within the amino acid sequence of SEQ ID NO: 4, wherein said polypeptide …. induces antibodies in a mammal that bind to said amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay'. Thus, the minimum required size of the polypeptide recited in the new claim 55 is 8 amino acids in length, which is required to induces antibodies in a mammal that bind to said amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of any strain of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. New claim 56 includes the limitations: 'immunogenic composition comprising an isolated polypeptide comprising an amino acid sequence having 90% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4, ….. wherein said polypeptide …. induces antibodies in a mammal that bind to said amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay'. Thus, the polypeptide recited in the new claim 56 encompasses a polypeptide having 90%, 91%, 92%, 93% and 94% sequence identity with SEQ ID NO: 4 and therefore encompasses a polypeptide other than SEQ ID NO: 2 and SEQ ID NO: 4 which is *required* to induce antibodies in a mammal that bind to said amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. Applicants state that support for the term 'epitope' and/or 'fragment' of the OMP85 sequence as used in claim 55, the minimal size limitation of at least 8 amino acids, and for the polypeptide having the ability to induce antibodies which interfere with adherence of *Neisseria gonorrhoeae* in the gonococcal cell adherence assay is found at page 20, line 25 to page 21, line 4 and in Example 8. Applicants contend that Example 8 provides a description of polypeptide containing an epitope of OMP85 within the first 178 amino acids of the N-terminal sequence of SEQ ID NO: 2, which is 95% identical to SEQ ID NO: 4. Applicants state that the limitation of 90% or greater sequence identity as recited in the new claim 56 finds support at page 19, lines 26-27 and in Figures 3, 4, 7A and 7B. However, these parts of the originally filed specification, do not provide descriptive support for any specific eight amino acid-long polypeptide or less than the first 178 amino acid-long polypeptide of SEQ ID NO: 4 that induce antibodies in a mammal that 'interfere with adherence of *Neisseria gonorrhoeae* in the gonococcal

cell adherence assay. Other than SEQ ID NO: 2 and a polypeptide comprising the first 178 amino acids of SEQ ID NO: 2, no other isolated polypeptides comprising an amino acid sequence having 90% or greater amino acid sequence identity with the amino acid sequence of SEQ ID NO: 4 are described to have the ability to induce antibodies in a mammal *which antibodies interfere with adherence of Neisseria gonorrhoeae in the gonococcal cell adherence assay*. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the new limitation(s), or alternatively remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Written Description)

14) Claims 25, 39-42, 44-46, 55, 56 and 58 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 25, as amended, is drawn to a 'diagnostic composition' comprising an isolated polypeptide having an amino acid of 95% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4, or having an amino acid sequence which comprises 'an epitope of said SEQ ID NO: 4', wherein the polypeptide is labeled. Claim 25 is thus drawn to a vast genus of isolated polypeptides having an amino acid of 95% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4, or having an amino acid sequence which comprises 'an epitope of said SEQ ID NO: 4' wherein the polypeptide species are required to have a diagnostic function. The new limitation 'an epitope of said SEQ ID NO: 4' has no size and/or structure limit, but is required to have diagnostic function, i.e., diagnosis of an unspecified disease or condition. The term 'epitope' encompasses a contiguous epitope and a discontiguous epitope, a

linear epitope and a conformational epitope, and a B-cell epitope and a T-cell epitope. Although claim 25 is drawn to a diagnostic composition comprising a labeled polypeptide as recited, the dependent claim 44-46 require that this labeled diagnostic polypeptide composition 'induce antibodies which recognize a protein in multiple *Neisseria gonorrhoeae* strains (FA19, FA635, FA1090, JS1, MS11 and F62) and *Neisseria meningitdis* strains (HH, MP78, MP3 and MP81)'. This means that the labeled diagnostic polypeptide composition of the dependent claims 44-46 are required to be 'immunogenic' as well, being capable of inducing broadly cross-reactive antibodies. New claim 55 is drawn to an 'immunogenic composition comprising an isolated polypeptide ……. said polypeptide comprising an epitope of at least 8 consecutive amino acids within the amino acid sequence of SEQ ID NO: 4, wherein said polypeptide …. induces antibodies in a mammal that bind to the amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay'. Thus, the minimum required size of the polypeptide recited in the new claim 55 is 8 amino acids in length, which is required to induce antibodies in a mammal that bind to said amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. New claim 56 is drawn to an 'immunogenic composition comprising an isolated polypeptide comprising an amino acid sequence having 90% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4, ….. wherein said polypeptide …. induces antibodies in a mammal that bind to said amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay'. Thus, the polypeptide recited in the new claim 56 encompasses a vast genus of polypeptides having 90%, 91%, 92%, 93% and 94% sequence identity with SEQ ID NO: 4 and therefore encompasses a polypeptide other than SEQ ID NO: 2 and SEQ ID NO: 4 and is *required* to induce antibodies in a mammal that bind to the amino acid sequence of SEQ ID NO: 4 and that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. The variations within the encompassed genus are huge. Any amino acids in any number and in any sequence along the length of SEQ ID NO: 4 may be substituted as long as there is at least 90% sequence identity to SEQ ID NO: 4. The specification intends diagnostic, therapeutic and vaccination (prophylactic) applications for the claimed polypeptide genus. See abstract.

The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The written description requirement can be met by describing the claimed subject matter to a person skilled in the art using sufficiently detailed, relevant identifying characteristics such as functional characteristics, and correlating those functional characteristics with a disclosed structure. See *Enzo Biochem v. Gen-Probe,* 323 F.3d 956, 964, 967, 968 (Fed. Cir. 2002). Sufficient description to show possession of a genus may be achieved by means of recitation of a representative number of peptides, defined by amino acid sequences falling within the scope of the genus, or recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may *not* be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

In the instant application, Applicants have shown possession of the Omp85 polypeptide sequence species of SEQ ID NO: 4 of *Neisseria meningitdis* HH and SEQ ID NO: 2 of *Neisseria gonorrhoeae* FA19. The disclosed structure or the amino acid sequences of the two polypeptide species, SEQ ID NO: 2 and 4, are depicted in the Sequence Listing and in Figure 5. SEQ ID NO: 2 is stated to be 95% identical to SEQ ID NO: 4. See the last sentence on page 6 of Applicants' amendment filed 05/01/08. However, the description of these two species within a claimed genus may not be sufficient to support the patentability of the vast genus having the requisite function under 35 U.S.C § 112, first paragraph. See *University of California v. Eli Lilly & Co.*, 119 F.3d 15559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). The specification does not disclose any isolated or purified Omp85 polypeptide variants in which the amino acid sequence of SEQ ID NO: 4 is varied to be at least 90% identical to SEQ ID NO: 4, wherein the at least 90% identical polypeptide variants have the recited *requisite* function, i.e., ability to be of diagnostic significance and the ability to induce antibodies that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. The instant specification does not disclose which 5-10% of amino acid residues should be changed within the disclosed polypeptide species

of SEQ ID NO: 4 in order to maintain the required biological functions, i.e., the diagnostic function and the ability to induce antibodies that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. There is lack of adequate description of the structure of a representative number of isolated 90% or 95% identical Omp85 polypeptide variant species having the recited requisite functions. It should be noted that written description requires more than a mere statement that something is a part of the invention. Applicants have not described what contiguous or discontiguous determinants, or conformational or non-conformational epitopes, or B-cell or T-cell epitopes of the claimed polypeptide variant are correlated with the required diagnostic function and the required ability to induce antibodies that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. What exactly is the claimed composition diagnostic for, is not recited in claim 25.

With respect to the written description requirement, while 'examples explicitly covering the full scope of the claim language' typically will not be required, a sufficient number of representative species must be included 'to demonstrate that the patentee possesses the full scope of the [claimed] invention'. *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). In the instant case, Applicants' specification does not contain adequate written description sufficient to show they had possession of the full scope of their claimed invention at the time the application was filed. The instant specification mentions of an isolated polypeptide having 90%, 95% or greater sequence identity to the amino acid sequence of SEQ ID NO: 4. See paragraph bridging pages 19 and 20 of the specification. The specification herein mentions of conservative variants of Omp85 polypeptide. However, the specification does not disclose a correlation between the function, i.e., the generic diagnostic function; specific meningococcal or gonococcal diagnostic function; and the ability to induce antibodies that recognize a protein in *Neisseria gonorrhoeae* strains, FA19, FA635, FA1090, JS1, MS11 and F62, and *Neisseria meningitdis* strains, HH, MP78, MP3 and MP81; and the ability to induce antibodies that interfere with adherence of any strain of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay, and the precise structure responsible for those functions. The precise structure of the at least eight amino acid long epitope or an epitope of SEQ ID NO: 4 of any size having such functions is not identified, such that a skilled artisan would have known what modifications, substitutions, or variations could be made of the large number of modifications or

variations currently encompassed within the scope of the instant claims without losing the requisite functions. Clearly, Applicants did not describe the invention of the instant claims adequately to show that they had possession of the claimed genus of isolated polypeptide variants or their epitopes. See e.g., *Noelle v. Lederman*, 355 F.3d 1343, 1348, 69 USPQ2d 1508, 1513 (Fed. Cir. 2004) ('invention is, for purposes of the written description inquiry, *whatever is now claimed*'). Applicants should note that written description requires more than a mere statement that something is a part of the invention and a reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The specification intends diagnostic, vaccination (prophylactic) and therapeutic applications for the claimed genus polypeptides. As known in the art of immunology, a diagnostic, immunogenic, cross-reactive, or adherent epitope can be contiguous or linear, or conformational or discontinuous, and it interacts with its corresponding antibody based on the three dimensional structure of both the molecules and the fit between the molecules. See page 46 of Cruse *et al.*, *Illustrated Dictionary of Immunology*, 2nd Edn., CRC Press, 2003. For an antibody to have the diagnostic, cross-reactive, and/or anti-adherent ability with or against a homologous or heterologous serotype or strain of *Neisseria gonorrhoeae* or *Neisseria meningitdis*, it has to bind immunospecifically with said homologous or heterologous serotype or strain of *Neisseria gonorrhoeae* or *Neisseria meningitdis*. The epitopes of bacterial polypeptides are known to be serogroup-specific, serotype-specific, immunotype-specific, subtype-specific, or strain-specific. The instant specification does not adequately describe or identify the linear or conformational epitopes that are broadly cross-reactive or specifically serotype-specific, non-serotype-specific, and/or strain-specific, within SEQ ID NO: 4, or within an amino acid sequence that is 90% or 95% identical to SEQ ID NO 4. This description is important because a change of even a single amino acid residue can alter the folding or conformation of a polypeptide such that the antibody-binding region no longer recognizes the polypeptide. See right column on page 33 of Colman PM. *Research Immunol.* 145: 33-36, 1994. The instant specification at paragraph bridging pages 19 and 20 mentions of conservative variants of an Omp85 polypeptide. However, it is recognized in the art that even a very conservative substitution may abolish binding. See first full paragraph on page 35 of Colman. Colman taught that binding interactions could be considered less tolerant because the

changes involved occur in what might be called the active site. See third full paragraph on page 35 of Colman.

Although a microbial polypeptide having at least 5-10% non-identity with the native polypeptide is expected in the art to generally induce some antibodies, the binding specificity of such antibodies to the native polypeptide and therefore their ability to be broadly cross-reactive with multiple strains of *Neisseria gonorrhoeae* and *Neisseria meningitdis* and their ability to interfere with adherence of any strain of *Neisseria gonorrhoeae* as measured by the gonococcal adherence assay, is not predictable. The art reflects unpredictability as to which amino acids in a specific protein or polypeptide can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific protein or polypeptide. In other words, the retention of the immunospecificity, cross-reactivity, and/or adherent ability following one or more amino acid substitutions within a bacterial polypeptide or within an epitope or fragment thereof, is not predictable. For instance, McGuinnes *et al*. (*Mol. Microbiol*. 7: 505-514, Feb 1993) taught that "[a] single amino acid change within an epitope, or an amino acid deletion outside an epitope, were both associated with loss of subtype specificity resulting from a change in the predicted conformation at the apex of the loop structure" in case of a meningococcal polypeptide (see abstract). Similarly, McGuinnes *et al*. (*Lancet* 337: 514-517, March 1991) taught that a point mutation generating a single amino acid change in a P1.16-specific epitope in the VR2 region of the *porA* gene of a strain of *Neisseria meningitidis* of subtype P1.7,16 resulted in "striking changes in the structural and immunological properties of the class 1 protein" of this isolate. See abstract and page 514 of McGuinnes *et al*. Thus, these prior art references document the unpredictability in obtaining a functional variant of a microbial polypeptide or peptide that retains its specific immunological binding function(s). In the instant case, the Omp85 polypeptide of SEQ ID NO: 4 is asserted to be a novel polypeptide of *Neisseria meningitdis*. However, what is claimed is not merely an isolated polypeptide of SEQ ID NO: 4. Applicants are claiming a vast genus of at least 90% to 95% identical isolated polypeptide variants of SEQ ID NO: 4 and their epitopes of any size, or epitopes at least 8 amino acids in length, wherein the isolated polypeptide variants or epitopes thereof are required to have the capacity to be diagnostic for an unspecified disease or condition, the capacity to induce antibodies that broadly recognize a protein in *Neisseria gonorrhoeae* strains, FA19, FA635, FA1090, JS1, MS11 and

F62, and *Neisseria meningitdis* strains, HH, MP78, MP3 and MP81; and/or the ability to induce antibodies that interfere with adherence of any strain of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. However, Applicants have not described which epiotpes of the claimed polypeptide variants are correlated with the required capacity to be diagnostic for an unspecified disease or condition, with the capacity to induce antibodies that broadly recognize a protein in *Neisseria gonorrhoeae* strains, FA19, FA635, FA1090, JS1, MS11 and F62, and *Neisseria meningitdis* strains, HH, MP78, MP3 and MP81; and/or with the ability to induce antibodies that interfere with adherence of any strain of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. Applicants have not described which of SEQ ID NO: 4's amino acids can be varied such that the polypeptide variant or the epitope thereof still maintains the above-identified functional capacities. Which epitopes within SEQ ID NO: 4 are *Neisseria gonorrhoeae*-specific, and/or *Neisseria meningitdis*-specific such that they can be of diagnostic significance in meningococcal and/or gonococcal diseases is not adequately described. This is critically important, because the instant specification at lines 16-19 of page 10 and Figure 5 expressly indicates that the Omp85 of SEQ ID NO: 4 contains therein epitope(s) shared by the D-15-Ag of *H. influenzae* and Oma87 protein of *Pasteurella multocida*. Such epitopes cannot be of specific diagnostic significance in meningococcal and/or gonococcal diseases. The state of the art indicates that SEQ ID NO: 4 contains several epitopes that are not specific to meningococci and/or gonococci, but are shared by a sequence of *Arabidopsis thaliana, Pyrococcus abyssi*, the *hyper-thermophilic archaebacterium Pyrococcus horikoshii OT3, Vibrio cholerae,* and *Bacillus subtilis.* See sequence alignments (A) to (E) set forth below:

(A) IMBP4
site-specific recombinase for integration and excision - Bacillus phage phi-105
C;Accession: T13541; C24521; D24521; E24521; F24521
R;Kobayashi, K.; Okamura, K.; Inoue, T.; Sato, T.; Kobayashi, Y.
submitted to the EMBL Data Library, July 1998
A;Description: Complete nucleotide sequence of Bacillus subtilis phage phi-105.
A;Reference number: Z17688
A;Accession: T13541
R;Cully, D.F.; Garro, A.J.
Gene 38, 153-164, 1985
A;Title: Nucleotide sequence of the immunity region of Bacillus subtilis bacteriophage phi-105: identification of the repressor gene and its mRNA and protein products.
A;Reference number: A91535; MUID:86056972; PMID:3934047
A;Accession: C24521
A;Residues: 1-78,'MTHC' <CUL>
A;Cross-references: GB:M11920; NID:g215477; PIDN:AAA88399.1; PID:g1196717
A;Accession: D24521

A;Residues: 149-160,'AR',163,'H','HSDSQRRVR',381-383,'RIQRRARS',392 <CU2>
A;Cross-references: GB:M11920; NID:g215477; PIDN:AAA88401.1; PID:g1196719
A;Accession: E24521
A;Residues: 189-318,'HAP' <CU3>
A;Cross-references: GB:M11920
A;Accession: F24521
  Query Match 1.0%; Score 8; DB 1; Length 474;
  Best Local Similarity 100.0%; Pred. No. 18;
  Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0

Qy 168 IDEGKSAK 175
        ||||||||
Db 53 IDEGKSAK 60

(B) A71175

probable dehydrogenase - Pyrococcus horikoshii

C;Species: Pyrococcus horikoshii

C;Date: 14-Aug-1998 #sequence_revision 14-Aug-1998 #text_change 12-Jul-2004

C;Accession: A71175

R;Kawarabayasi, Y et al.

DNA Res. 5, 55-76, 1998

A;Title: Complete sequence and gene organization of the genome of a hyper-thermophilic archaebacterium, Pyrococcus horikoshii OT3.

A;Reference number: A71000; MUID:98344137; PMID:9679194

A;Accession: A71175

A;Status: preliminary; nucleic acid sequence not shown; translation not shown

A;Cross-references: UNIPROT:O58320; GB:AP000002; NID:g3236129; PIDN:BAA29686.1; PID:g3257003

  Query Match 1.0%; Score 8; DB 2; Length 376;

  Best Local Similarity 100.0%; Pred. No. 15;

  Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0

Qy 485 LGYDVYGK 492

        ||||||||

Db 186 LGYDVYGK 193

(C) C82190

Formate dehydrogenase accessory protein VC1519 [imported] - Vibrio cholerae (strain N16961 serogroup O1)

C;Species: Vibrio cholerae

C;Date: 18-Aug-2000 #sequence_revision 20-Aug-2000 #text_change 09-Jul-2004

C;Accession: C82190

R;Heidelberg, et al.

Nature 406, 477-483, 2000

A;Title: DNA Sequence of both chromosomes of the cholera pathogen Vibrio cholerae.

A;Reference number: A82035; MUID:20406833; PMID:10952301

A;Accession: C82190

A;Status: preliminary

A;Cross-references: UNIPROT:Q9KRW5; GB:AE004230; GB:AE003852; NID:g9656018; PIDN:AAF94673.1; GSPDB:GN00126; TIGR:VC1519

A;Experimental source: serogroup O1; strain N16961; biotype El Tor

C;Superfamily: formate dehydrogenase accessory protein FdhD

Query Match 1.0%; Score 8; DB 2; Length 337;

Best Local Similarity 100.0%; Pred. No. 14;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy        671 VYDEYGEK 678
              ||||||||
Db         81 VYDEYGEK 88
```

(D) B75057

glycerate dehydrogenase PAB2374 - Pyrococcus abyssi (strain Orsay)

C;Species: Pyrococcus abyssi

C;Date: 20-Aug-1999 #sequence_revision 20-Aug-1999 #text_change 09-Jul-2004

C;Accession: B75057

R;anonymous, Genoscope

submitted to the EMBL Data Library, July 1999

A;Description: Pyrococcus abyssi genome sequence: insights into archaeal chromosome structure and evolution.

A;Reference number: A75001

A;Accession: B75057

A;Status: preliminary

A;Cross-references: UNIPROT:Q9UYR1; GB:AJ248287; GB:AL096836; NID:g5458657; PIDN:CAB50351.1; PID:g5458864

A;Experimental source: strain Orsay

Query Match 1.0%; Score 8; DB 2; Length 335;

Best Local Similarity 100.0%; Pred. No. 14;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0

```
Qy        485 LGYDVYGK 492
              ||||||||
Db        145 LGYDVYGK 152
```

(E) E84423

hypothetical protein At2g01340 [imported] - Arabidopsis thaliana

C;Species: Arabidopsis thaliana (mouse-ear cress)

C;Date: 02-Feb-2001 #sequence_revision 02-Feb-2001 #text_change 09-Jul-2004

C;Accession: E84423

R;Lin X et al. Nature 402, 761-768, 1999

```
A;Title: Sequence and analysis of chromosome 2 of the plant Arabidopsis thaliana.
A;Reference number: A84420; MUID:20083487; PMID:10617197
A;Accession: E84423
A;Status: preliminary
A;Cross-references: UNIPROT:Q9ZU33; GB:AE002093; NID:g4262241; PIDN:AAD14534.1;
GSPDB:GN00139
  Query Match             1.0%;  Score 8;  DB 2;  Length 225;
  Best Local Similarity   100.0%;  Pred. No. 9.5;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0
Qy        280 PKAELEKL 287
              ||||||||
Db        144 PKAELEKL 151
```

Clearly, Applicants have not identified one or more epitopes of any size, or eight amino acid-long or shorter epitopes that are of specific diagnostic value in meningococcal and/or gonococcal diseases, or that induce antibodies which interfere with adherence of any strain of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay. Without a concrete structure-function correlation, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ….. does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). The instant claims are viewed as not meeting the written description provision of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C § 102

15) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

16) Claims 25, 39-42, 44-46 and 55 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Rubenfield *et al.* (US 6,551,795, filed 02/18/1998, already of record) as evidenced by Harlow *et al.* (*In*: *Antibodies: A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988, already of record).

It is noted that the limitation 'epitope' in the independent claim 25 does not have a size or structure limit.

The transitional limitations 'having' or 'comprising', similar to 'including', 'containing', or 'characterized by', represent open-ended claim language and therefore, do not exclude additional, unrecited elements. See MPEP 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('comprising' leaves 'the claim open for the inclusion of unspecified ingredients even in major amounts'). Therefore, the limitation 'comprising' or 'contains' in the instant claim(s) allows additional amino acid residues to be present on one or either side of the recited polypeptide, or an epitope thereof. It should be noted that the transitional phrase 'consisting of' excludes any element, step, or ingredient not specified in the claim. *In re Gray, 53 F.2d 520, 11 USPQ 255 (CCPA 1931)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('consisting of' defined as 'closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith.').

Rubenfield *et al.* disclosed an isolated or a substantially pure 648 amino acid-long polypeptide having the amino acid sequence of SEQ ID NO: 24628 comprising the eight consecutive amino acids, VRVETADG, which eight consecutive amino acids are identical to the eight amino acid-long fragment, VRVETADG, located at amino acid positions 74 through 81 of the instantly recited SEQ ID NO: 4, i.e., an eight amino acid-long epitope located within the first 178 amino acid-long N-terminal sequence of SEQ ID NO: 4 that is used in Example 8 of the instant specification. A therapeutic or prophylactic vaccine comprising the polypeptide and a pharmaceutically acceptable carrier as well as a diagnostic composition, a diagnostic reagent capable of providing a detectable signal comprising the polypeptide modified with a label, such as a radioisotope or a fluorescent label, is taught. A diagnostic kit comprising the polypeptide being

present on immobilization means such as particles, supports (inclusive of latex), wells, dipsticks, and the nitrocellulose papers containing the polypeptide, is also disclosed. The polypeptide exists as a recombinant fusion protein fused to a polyhistidine sequence, i.e., fused to a second heterologous protein or polypeptide. The polypeptide is co-administered with an adjuvant. See Sequence Listing; third full paragraph in column 5; first three paragraphs in column 6; lines 18-29 in column 11; and 'Vaccine Formulations for P. aeruginosa .... Polypeptides' in columns 37-40; section 'Kits Containing ... Polypeptides of the Invention'; and lines 1-5 of column 42. See also the sequence alignment below:

```
US-09-252-991A-24628
Sequence 24628, Application US/09252991A
Patent No. 6551795
GENERAL INFORMATION:
APPLICANT:  Marc J. Rubenfield et al.
TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO PSEUDOMONAS
TITLE OF INVENTION:  AERUGINOSA FOR DIAGNOSTICS AND THERAPEUTICS
FILE REFERENCE:  107196.136
CURRENT APPLICATION NUMBER: US/09/252,991A
CURRENT FILING DATE:  1999-02-18
PRIOR APPLICATION NUMBER:  US 60/074,788
PRIOR FILING DATE:  1998-02-18
PRIOR APPLICATION NUMBER:  US 60/094,190
PRIOR FILING DATE:  1998-07-27
NUMBER OF SEQ ID NOS:  33142
SEQ ID NO 24628
LENGTH: 648
TYPE: PRT
ORGANISM: Pseudomonas aeruginosa
US-09-252-991A-24628
Query Match              1.0%;  Score 8;  DB 4;  Length 648;
Best Local Similarity   100.0%;  Pred. No. 35;
Matches  8;  Conservative  0;  Mismatches  0;  Indels  0;  Gaps 0

Qy         74 VRVETADG 81
              ||||||||
Db         94 VRVETADG 101
```

Since the isolated prior art polypeptide is not fully purified, it is expected to inherently contain at least a second *P. aeruginosa* protein or polypeptide contaminant, i.e., second polypeptide or protein antigen from a pathogenic species heterologous to *Neisseria meningitidis* or *Neisseria gonorrhoeae*. That the 648 amino acid-long prior art polypeptide containing therein the 8 amino acid-long epitope, VRVETADG, induces antibodies which bind to the instant polypeptide of SEQ ID NO: 4 or any other neisserial protein that contains the epitope as recited in the instant claim 55 is inherent from the teachings of the prior art, since such a polypeptide is well known in the art to be long enough to elicit an antibody response in a mammal. The art recognizes that the smallest

peptides that elicit antibodies which bind to the original full-length protein are 6 amino acids in length. See first sentence under 'Size of the Peptide' on page 76 of Harlow *et al.* Furthermore, although Rubenfield *et al.* are silent about the ability of their eight consecutive amino acid-containing polypeptide to induce antibodies in a mammal that interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay as recited in the instant claim 55 as recited in the instant claims, the prior art polypeptide is viewed as the same as the Applicants' polypeptide because of the identical structural composition. In spite of the fact that the prior art fails to teach all of the disclosed functional characteristics of the Applicants' polypeptide, there is total structural overlap to conclude that the prior art eight consecutive amino acid-containing epitope falls well within the first 178 amino acids of the instantly recited SEQ ID NO: 4 is one and the same as the Applicants' eight consecutive amino acid-containing epitope. Since the prior art eight consecutive amino acid-long epitope is structurally the same as the epitope recited in the instant claims and is an epitope contained within the first 178 amino acids of SEQ ID NO: 2 that is used to induce antibodies in Example 8 of the instant specification, it is expected to necessarily have the same intrinsic binding and adherence-interfering properties as that of the Applicants' epitope or polypeptide, absent evidence to the contrary.

The teachings of Rubenfield *et al.* anticipate the instant claims 25, 30-36, 39-42, 44-46 and 55. Harlow *et al.* is **not** used as a secondary reference in combination with Rubenfield *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Rubenfield *et al.* with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

17) Claims 50, 52, 55, 56 and 30-36 are rejected under 35 U.S.C § 102(b) as being anticipated by Dunn *et al.* (*Microbial Pathogenesis* 18: 81-96, 1995) as evidenced by Mignogna *et al.* (*J. Proteome Res.* 4: 1361-1370, 2005).

It is noted that Exhibit C of the Judd declaration submitted filed 02/06/05 documents that MC58 strain of *Neisseria menigitidis* produces the OMP85 polypeptide that has greater than 95% sequence identity with the instantly recited polypeptide of SEQ ID NO: 4.

Dunn *et al.* taught a composition comprising isolated outer membrane vesicles (OMV) from the MC58 strain of *N. meningitidis* contained in PBS buffer (i.e., a pharmaceutically

acceptable carrier). See paragraph above the section 'Cytotoxicity assay' on page 93. That the prior art OMV composition comprises the Omp85 protein of MC58 strain of *N. meningitidis* is inherent from the teachings of Dunn *et al.* in light of what is known in the art. For instance, Mignogna *et al.* teach that MC58 strain of *N. meningitidis* does produce the Omp85 protein. See spot number 12a in Table 1. Since the prior art OMV composition is not detergent-purified, it is expected to contain other cell-free (i.e., isolated from the cellular mass of the MC58 *N. meningitidis*) LPS, antigenic proteoglycan, or other protein antigenic contaminats of the MC58 *N. meningitidis* naturally fused thereto.

Claims 50, 52, 55, 56 and 30-36 are anticipated by Dunn *et al.* Mignogna *et al.* is **not** used as a secondary reference in combination with Dunn *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Dunn *et al.* See *In re Samour* 197 USPQ (CCPA 1978).

18) Claims 25, 39-42 and 44-46 are rejected under 35 U.S.C § 102(b) as being anticipated by Chong *et al.* (WO 94/12641, already of record) ('641) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988, already of record).

It is noted that the limitation 'epitope' in the independent claim 25 does not have a size or structure limit.

The transitional limitations 'having' or 'comprising', similar to 'including', 'containing', or 'characterized by,' represent open-ended claim language and therefore, do not exclude additional, unrecited elements. See MPEP 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('comprising' leaves 'the claim open for the inclusion of unspecified ingredients even in major amounts'). Therefore, the limitation 'comprising' or 'contains' in the instant claim(s) allows additional amino acid residues to be present on one or either side of the recited polypeptide, or a homolog thereof. It should be noted that the transitional phrase 'consisting of' excludes any element, step, or ingredient not specified in the claim. *In re Gray, 53 F.2d 520, 11 USPQ 255 (CCPA 1931)*; *Ex parte Davis, 80*

USPQ 448, 450 (Bd. App. 1948) ('consisting of' defined as 'closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith.').

Chong *et al*. disclosed an isolated and purified 27 amino acid-long fragment, SEQ ID NO: 35, or a synthetic peptide of the D-15 polypeptide fused to a heterologous protein, such as, glutathione S-transferase, i.e., second heterologous polypeptide. The prior art polypeptide comprises the sequence, DGVSLGGN, of which DGVSLG is 100% identical to amino acids 481-486 of the instantly claimed polypeptide of SEQ ID NO: 4. See Table 2 of Chong *et al*. The amino acids glycine and asparagine occurring at the carboxyl end of the DGVSLG prior art sequence represent two conservative amino acid replacements of tyrosine and aspartic acid in the eight amino acid-long sequence of DGVSLGYD found at positions 480-488 of the instantly recited SEQ ID NO: 4. Therefore, the prior art polypeptide of SEQ ID NO: 35 is viewed as an epitope of the instantly recited SEQ ID NO: 4. The polypeptide sequence is present in a physiologically acceptable carrier, and is highly immunogenic and elicits protective antibodies in a rabbits upon immunization with 50 to 200 micrograms in Freund's complete adjuvant (i.e., immunogenic composition). The polypeptide is useful as a diagnostic antigen for the purpose of diagnosis and is used in ELISA, RIAs and *other antibody binding assays or procedures known in the art*. A diagnostic kit comprising the polypeptide sequence is taught. See abstract; claims 13, 20, 21-23 and 28-31; SEQ ID NO. 35 in Table 2; paragraph bridging pages 3 and 4; paragraph bridging pages 5 and 6; first and second full paragraphs on page 6; Figures 9, 10 and 16; section iii on pages 12 and 13; sections vii, viii, ix-xiv; Examples 12 and 15; section 2 on page 31; and pages 24-28. The antibodies induced by Chong's isolated and purified 27 amino acid-long fragment, SEQ ID NO: 35, or the fusion protein thereof, contained in a physiologically acceptable carrier, are expected to have the functional properties recited in the instant claims, i.e., reactivity with multiple *Neisseria* strains that express a protein comprising the epitope, because the art recognizes that the smallest peptide which elicits antibodies that bind to the original full length protein is 6 amino acids in length. See first sentence under 'Size of the Peptide' on page 76 of Harlow *et al*. That the prior art polypeptide diagnostic antigen used in ELISA, RIAs and *other antibody binding assays or procedures known in the art*, contains a detection system or detectable label and is associated with nitrocellulose paper or a latex bead is inherent from the teachings of Chong *et al*.

The teachings of Chong *et al.* anticipate the instant claims 25, 39-42 and 44-46. Harlow *et al.* is **not** used as a secondary reference in combination with Chong *et al*, but rather is used to show that every element of the claimed subject matter is disclosed by Chong *et al.* with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

19) Claims 50, 52, 55 and 56 are rejected under 35 U.S.C § 102(b) as being anticipated by West *et al.* (*Infect. Immun.* 47: 388-394, 1985) as evidenced by Manning *et al.* (*Microb. Pathogenesis*. 25: 11-22, July 1998, already of record) (Manning *et al.*, 1998).

It is noted that the Omp85 polypeptide of SEQ ID NO: 2, which has 95% sequence identity with the instantly recited SEQ ID NO: 4, is isolated from FA19 strain of *Neisseria gonorrhoeae*. See Figure 5 of the instant specification.

West *et al.* taught an outer membrane composition comprising a buffer (i.e., pharmaceutically acceptable carrier) and at least one isolated polypeptide or protein from FA19 strain of *Neisseria gonorrhoeae* having a molecular weight of approximately 85 kDa as measured by SDS PAGE. See 'Materials and Methods', particularly the first and the last two full paragraphs under 'Materials and Methods'; and Figures 1 and 2. The isolated Omp85-containing prior art outer membrane composition from FA19 strain of *Neisseria gonorrhoeae* is expected by those of skill in the art to be immunogenic and induce antibodies in a mammal. The prior art composition anticipates the instant claims since it intrinsically comprises the isolated SEQ ID NO: 2 of the same FA19 strain of *Neisseria gonorrhoeae* that is described in the instant specification under 'Brief Description of the Drawings' for Figures 3 and 6. That the Omp85 contained in the prior art outer membrane composition from FA19 strain of *Neisseria gonorrhoeae* has an amino acid sequence having 95% sequence identity with the instantly recited SEQ ID NO: 4 is inherent from the teachings of West *et al.* in light of what is known in the art. For instance, Manning *et al.* (1998) show that the Omp85 polypeptide from FA19 strain of *Neisseria gonorrhoeae* has an amino acid sequence having 95% sequence identity with the instantly recited SEQ ID NO: 4. See Figures 5 and 1; first two full paragraphs on page 15; second and third full paragraphs under 'Materials and Methods'. The Office's position that the prior art composition is the same as the instantly claimed composition is based on the fact that the prior art FA19 strain of *Neisseria gonorrhoeae* is the

same strain of Applicants that is used in Example 1 of the instant specification. The ability to induce antibodies in a mammal as recited in the instant claims which interfere with adherence of *Neisseria gonorrhoeae* as measured by the gonococcal cell adherence assay is viewed as an inherent functional property inseparable from the prior art polypeptide comprised in West's immunogenic OMV composition.

The teachings of West *et al*. anticipate the instant claims 50, 52, 55 and 56. Manning *et al*. (1998) is **not** used as a secondary reference in combination with West *et al*., but rather is used to show that every element of the claimed subject matter is disclosed by West *et al*. with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

Relevant Prior Art

20) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Manning *et al*. (Manning *et al*., May 1997) disclosed an outer membrane protein, Omp85, of *Neisseria meningitidis* and its amino acid sequence, SEQ ID NO: 4. The polypeptide comprises a fragment of SEQ ID NO: 4. See sequence alignment below:

```
P95359
ID   P95359      PRELIMINARY;      PRT;   792 AA.
AC   P95359;
DT   01-MAY-1997 (TrEMBLrel. 03, Created)
DT   01-MAY-1997 (TrEMBLrel. 03, Last sequence update)
DT   01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DE   Outer membrane protein.
GN   Name=omp85;
OS   Neisseria gonorrhoeae.
OC   Bacteria; Proteobacteria; Betaproteobacteria; Neisseriales;
OC   Neisseriaceae; Neisseria.
OX   NCBI_TaxID=485;
RP   SEQUENCE FROM N.A.
RC   STRAIN=FA19;
RX   MEDLINE=98379445; PubMed=9705245; DOI=10.1006/mpat.1998.0206;
RA   Manning D.S., Reschke D.K., Judd R.C.;
RT   "Omp85 proteins of Neisseria gonorrhoeae and Neisseria meningitidis
RT   are similar to Haemophilus influenzae D-15-Ag and Pasteurella
RT   multocida Oma87."
RL   Microb. Pathog. 25:11-21(1998).
DR   EMBL; U81959; AAC17600.1; -.
DR   InterPro; IPR000184; Bac_surfAg_D15.
DR   InterPro; IPR010827; Surf_Ag_VNR.
DR   Pfam; PF01103; Bac_surface_Ag; 1.
DR   Pfam; PF07244; Surf_Ag_VNR; 5.
SQ   SEQUENCE   792 AA;  87868 MW;  90E32D24AA0513D8 CRC64
```

```
  Query Match             19.7%;  Score 157;  DB 2;  Length 792;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-150;
  Matches  157;  Conservative  0;  Mismatches  0;  Indels  0;  Gaps  0

Qy        332 TKTVDFVLHIEPGRKIYVNEIHITGNNKTRDEVVRRELRQMESAPYDTSKLQRSKERVEL 391
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        332 TKTVDFVLHIEPGRKIYVNEIHITGNNKTRDEVVRRELRQMESAPYDTSKLQRSKERVEL 391

Qy        392 LGYFDNVQFDAVPLAGTPDKVDLNMSLTERSTGSLDLSAGWVQDTGLVMSAGVSQDNLFG 451
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        392 LGYFDNVQFDAVPLAGTPDKVDLNMSLTERSTGSLDLSAGWVQDTGLVMSAGVSQDNLFG 451

Qy        452 TGKSAALRASRSKTTLNGSLSFTDPYFTADGVSLGYD 488
              |||||||||||||||||||||||||||||||||||||
Db        452 TGKSAALRASRSKTTLNGSLSFTDPYFTADGVSLGYD 488
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Remarks

21) Claims 25, 30-36, 39-42, 44-46, 50, 52 and 55-58 stand rejected.

22) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Central Fax number (571) 273-8300, which receives facsimile transmissions 24 hours a day and 7 days a week.

23) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

24) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Shanon Foley, can be reached on (571) 272-0898.

/S. Devi/
S. Devi, Ph.D.
Primary Examiner
AU 1645

July, 2008